

## REMARKS

This Amendment and Response is submitted in response to the Office Action mailed 5 February 2004. Withdrawal of the rejection and reconsideration with an eye toward allowance is respectfully requested.

### Claim Status

Claims 2-3, 5-9, 24-34, and 36-41 are pending after entry of the present amendment. Claims 2, 3, 5-9 and 24-34 stand rejected. Claims 25 and 26 are amended herein. Claim 35 is withdrawn. Claims 36-41 are added herein. A complete listing of all claims that are, or were in the application, along with an appropriate status identifier, is provided above in the section entitled "Amendments to the Claims". Markings are provided on claims amended in the present amendment.

Support for the amendments and new claims can be found throughout the originally filed specification, drawings, and claims. See, for example page 13, lines 8-11 and pages 17-18, 23, and 25.

### Election/Restriction

The Examiner suggests that newly submitted claim 35 is directed to an invention that is independent or distinct from the invention originally claimed. Without conceding the propriety of the restriction, Applicant has indicated claim 35 as withdrawn.

### Claim Rejections – 35 U.S.C. §112

Claim 34 was rejected under 35 U.S.C. §112, second paragraph, as failing to comply with the written description requirement. The Examiner suggests that the claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention. Applicant respectfully disagrees and directs the Examiner's attention to page 14, line 16, which clearly indicates "the cap can be designed to be removable".

Accordingly, Applicant respectfully submits that claim 34 complies with the written description requirement of 35 U.S.C. §112, second paragraph.

### Claim Rejections – 35 U.S.C. §102

Claims 24, 2, 3, 5, 7, and 8 were rejected under 35 U.S.C. §102(e) as being anticipated by Burns et. al. (U.S. Patent No. 6,379,929).

Applicant notes that an identical rejection was contained in the Final Office Action mailed July 23, 2004, and addressed by Applicant in the response filed November 19, 2003. Applicant respectfully

submits that Burns fails to disclose "a substrate comprising a printed circuit board comprising an array of electrodes, each electrode comprising: A) a self-assembled monolayer; and B) a capture binding ligand." Applicant's arguments of November 19, 2003 are incorporated again herein by reference.

The Examiner's suggests that "a careful reading of the cited passage reveals that Burn et. al. teach the channel comprises electrodes and the surface of the channel is coated with the self-assembled monolayer" (see office action, page 6).

Applicant respectfully submits that independent claim 24 recites electrodes, each electrode comprises a self-assembled monolayer and a capture binding ligand. Burns does not disclose such an electrode.

Taken as a whole, Burns is directed toward a microfabricated substrate or housing defining at least a first transport channel, or microdroplet transport channel, operably connected to at least a first reaction chamber, and at least a first means for isothermally regulating the temperature of the reaction chamber (see col. 3, line 67 – col. 4, line 4). Burns accordingly discloses fluid-directing means systems for use in the invention including those that employ a surface-tension-gradient mechanism in which discrete droplets are differentially heated and propelled through etched channels (see col. 6, lines 46-49). Differences in hydrophobic and hydrophilic surface structures may also be employed to control the flow or transport of fluids through the defined channels and etched components (see col. 7, lines 5-9).

Burns discloses channels made of diffused silicon on the bottom and a thin film cap on the top (col. 24, lines 51-52). On the top layer, a set of thin film electrodes and heaters is constructed (col. 24, lines 54-55). Burns discloses "surface treatment of the channels", in col. 26, lines 59-60 by "immersing the open channel in organosilane or a self-assembled monolayer coating". Applicant respectfully submits that by immersing the "open channel" in a self-assembled monolayer coating, the "top layer" containing the set of thin film electrodes would not be exposed to the self-assembled monolayer coating, resulting in a surface treatment applied to a channel during a period where the electrodes are removed from the channel. Accordingly, applicant submits that the electrodes would not comprise a SAM.

Burns discloses electrodes for the purpose of providing heaters and temperature detectors (see col. 28, Section 'E'). In col. 29, lines 1-22, Burns discloses patterning of a silicon oxide substrate designed to pattern hydrophobic regions onto a hydrophilic silicon oxide surface, where the silicon oxide surface has openings to metal contact pads. Applicant notes that a self-assembled monolayer coating is here applied to an oxide surface, and the SAM on the chromium metal gets lifted off, see col. 29 line 17. Burns does not disclose an electrode comprising a SAM.

Burns further fails to disclose an electrode comprising a capture binding ligand. The Examiner points to Burns, col. 47, lines 12-26, which reads as follows, "In certain embodiments one or more of the reagents, nucleotides, buffers, salts, chemicals, solvents, primers, target nucleic acids including DNA and/or RNA, polymerases, endonucleases, nucleases, and chemical or biological components suitable for the isothermal reaction mixture are added to the at least first and/or second microdroplet transport channels separately or in various combinations. In other preferred embodiments of the invention one or

more of the nucleotides, buffers salts, chemicals, solvents, primers, target nucleic acids including DNA and/or RNA, polymerases, endonucleases, nucleases, and chemical or biological components suitable for an isothermal amplification reaction are contained in, in liquid communication with, operably or functionally connected to, and/or provided with the microfabricated structure.” Of particular relevance to the Examiner is Burns’ disclosure that one or more of these reagents may be operably or functionally connected to the microfabricated structure.

In the present case, Applicant has recited an electrode comprising a capture binding ligand, while Burns discloses a reagent that may be operably or functionally connected to a microfabricated structure. Applicant submits that Burns fails to disclose the invention in as complete detail as is contained in Applicant’s claim 24. In particular, Burns fails to disclose an electrode comprising a capture binding ligand. Applicant respectfully submits that anticipation requires that “the identical invention must be shown in as complete detail as is contained in the patent claim” *Richardson v. Suzuki Motor Co. Ltd.* 9 USPQ2d 1913, 1920 (1989), *Jamesbury Corp. v. Litton Industrial Products, Inc.* 220 USPQ 253, 256 (Fed. Cir. 1985), *Connell v. Sears, Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983).

The Examiner suggests that “because Burns et al teach the channel comprises electrodes and binding ligands are functionally or operably connected to the channel, they teach the electrodes comprising binding ligands as claimed” (see office action, page 6). Applicant respectfully disagrees. Burns discloses an electrode exposed to a channel and reagents functionally or operably connected to a microfabricated structure. Burns does not disclose the elements as arranged in Applicant’s claim 24, namely an electrode comprising a self-assembled monolayer and a capture binding ligand. Anticipation requires that every element of the claimed invention must be literally present, arranged as in the claim. *Richardson v. Suzuki Motor Co. Ltd.* 9 USPQ2d 1913, 1920 (1989), *Perkin-Elmer Corp. v. Computervision Corp.* 221 USPQ 669, 673, *Kalman v. Kimberly-Clark Corp.*, 218 USPQ 781, 789 (Fed. Cir. 1983).

### **Claim Rejections – 35 U.S.C. §103**

Claim 6 and 2, 3, 5, 7, 8, and 31-33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski (U.S. Patent Number 6,051,380) in view of Eckhardt et. al. (U.S. Patent Number 5,945,334) and Besemer et. al. (U.S. Patent Number 5,945,334). Applicant respectfully traverses. Applicant submits that the proposed modification or combination would change the principle of operation of at least Sosnowski.

Sosnowski is directed toward addressed devices. Analytes or reactants can be transported by free field electrophoresis to any specific microlocation where the analytes or reactants are effectively concentrated and reacted with the specific binding entity and the microlocation (see col. 7, lines 62-66).

Eckhardt is directed toward an electrode for detecting interactions between members of a binding pair, which electrode has been modified by formation of a non-conductive self-assembled monolayer (see Abstract).

Besemer is directed toward a body having a cavity for mounting a chip (see abstract).

The Examiner suggests that It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the binding surface of Sosnowski et. al. with the SAM of Eckhardt. (see office action, page 7). Applicant respectfully disagrees. Applicant notes that "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." see MPEP §2143.01.

Sosnowski is concerned with the electrophoretic transport of analytes, see col. 9, lines 54-58 stating: "It should be emphasized that the primary function of the micro-electrodes used in these devices is to provide electrophoretic propulsion of binding and reactant entities to specific locations." The Sosnowski reference discloses the Sosnowski electrode further includes a permeation layer, "the permeation layer provides spacing between the metal surface and the attachment/binding entity layers and allows solvent molecules, small counter-ions, and electrolysis reaction gases to freely pass to and from the metal surface" (see col. 22, lines 1-4). In contrast, Eckhardt discloses an electrode with a self-assembled monolayer, stating: "Thus, the self-assembled monolayer is non-conductive, serves to immobilize reactants near the electrode surface, and allows the transition metal complex to move freely from the immobilized reactants to the conductive working surface of the electrode to permit electron transfer." (see Eckhardt, col. 5, lines 18-22).

Accordingly, one skilled in the art combining the binding surface of Sosnowski with the SAM of Eckhardt would change the principle of operation of the Sosnowski device which is clearly designed to provide electrophoretic propulsion of binding and reactant entities. That electrophoretic propulsion requires the ability for solvent molecules, small counter-ions, and electrolysis reaction gases to freely pass to and from the surface. Accordingly, coating the electrode of Sosnowski with the non-conductive SAM of Eckhardt would serve to block the transport of these solvent molecules, small counter-ions, and electrolysis reaction gases, halting the electrophoretic transport of binding and reactant entities, and rendering the Sosnowski electrode unfit for its primary function. For at least this reason, Applicant submits that the combination of Sosnowski and Eckhardt teachings are insufficient to render Applicant's independent claim 6 *prima facie* obvious. Claims 2, 3, 5, 7, 8, and 31-33 depend from and include all limitations of Applicant's independent claim 6 and are accordingly patentable over the cited art at least for the reasons described with regard to claim 6.

With further regard to claim 8, Applicant recites "wherein two surfaces of said substrate each comprise an array". The Examiner suggests that Sosnowski discloses a cartridge comprising two surfaces each comprising an array (see office action, page 8). Applicant respectfully disagrees. The Examiner points to Sosnowski at col. 23, lines 62-67. Here Sosnowski states that, "The 'chip' can be mounted in a standard quad package, and the chip contact pads wired to the quad package pins. Systems containing more than one chip and additional packaging and peripheral components may be designed to address problems related to clinical diagnostics...". It is unclear how the Examiner interprets

this disclosure as disclosure of two surfaces of a substrate each comprising an array. First, Applicant respectfully submits that a "quad package" simply refers to a package having pins along all four sides (see Sosnowski, Fig. 3). However, the chip shown in FIG. 3 contains only a single array. Applicant submits herewith Exhibit 1, a copy of the 'P' section of a dictionary available from Fujitsu and downloaded by the undersigned from <http://www.fme.fujitsu.com/dictionary/p.html>. The definition of PLCC – (Plastic Leaded Chip Carrier) is listed as a leaded quad package – a replacement for the plastic DIP (dual in-line package) in surface-mount applications. External connections consist of leads around all four sides of the package. Accordingly, Applicant submits that disclosure of a quad package by Sosnowski does not disclose two surfaces of a substrate each comprising an array, as recited in Applicant's claim 8. Further, while Sosnowski discloses that more than one chip may be provided with additional packaging, Sosnowski does not disclose two arrays on a same substrate. Accordingly, Applicant submits that claim 8 is further patentable over the cited art for at least this reason.

Claims 9, 34, and 25 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski in view of Eckhardt and Besemer as applied to claim 6 and further in view of Anderson et. al. (U.S. Patent Number 6,326,211).

As discussed above with regard to claim 6, Applicant respectfully submits that the combination of Sosnowski and Eckhardt as contemplated by the Examiner renders the device of at least Sosnowski inoperable. Claims 9, 34, and 25 depend from and include all limitations of Applicant's claim 6, and Applicant submits that the claims are patentable at least for the reasons discussed with regard to claim 6.

Anderson discloses a device for performing sample acquisition and preparation operations (see Anderson, col.5, lines 12-14). Data is gathered from the array by exciting fluorescently labeled targets (see Anderson, col. 16, lines 62-65).

Applicants respectfully submit that Sosnowski, Eckhardt and Anderson fail to provide the required motivation to combine the references. The combination of Sosnowski and Eckhardt has been discussed. With regard to the further combination of Anderson, the Examiner suggests that the motivation would be for the expected benefit of easy access to reagents and convenient storage of reagents, or for controlling fluid flow (see office action, page 10). Applicants respectfully submit that a convenient storage well for reagents, as disclosed by Anderson, is not necessarily a motivation to combine that storage well with the disclosure of Sosnowski and Eckhardt. "The mere fact that it is possible to find two isolated disclosures which might be combined in such a way to produce a new compound does not necessarily render such production obvious unless the art also contains something to suggest the desirability of the proposed combination." *In re Bergel*, 130 USPQ 206, 208 (CCPA 1961). Applicants submit that no specific motivation has been provided to combine a storage well or a valve as disclosed by Anderson, with the device of Sosnowski and/or Eckhardt. Accordingly, Applicants submit that the 35 U.S.C. §103(a) rejection of claims 9, 34, and 25 is improper and should be withdrawn.

With regard to claim 9, Applicant further submits that the references, taken alone or in combination, fail to disclose or suggest a "cap comprising at least one storage well comprising assay reagents," as recited in claim 9. The Examiner concedes that Sosnowski fails to disclose a cap (see office action, page 9), and relies on Anderson for disclosure of a cap. However, Applicant respectfully disagrees that Anderson discloses a "cap comprising at least one storage well comprising assay reagents," as recited in Applicant's claim 9.

The Examiner suggests that Anderson teaches a cap, referring to well #510 in Anderson's Fig. 5B. Applicants respectfully submit, as stated in Applicant's previous response, that Anderson merely discloses a well for holding reagent, and not a cap comprising a storage well, as recited by Applicant's claim 9. Claim 34 depends from and includes all limitations of Applicant's claim 9, further reciting that the cap is removable. The Examiner suggests that disassembly of the cartridge would remove the cap, thereby providing a removable cap (see office action, page 10). Applicant respectfully submits that such cartridge disassembly is not taught or suggested by the cited art, and respectfully requests that, should the Examiner maintain such a rejection, that the Examiner provide documentary support for the disassembly of the Anderson device (see MPEP §2144.03).

Claims 24 and 2, 7, 8, and 31 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski in view of Eckhardt. Applicant respectfully traverses, for at least the reasons described above with regard to claim 6 and the combination of Sosnowski and Eckhardt being unsuitable.

Claims 3, 5, 32, and 33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski in view of Eckhardt as applied to claim 24 and further in view of Besemer. Applicant respectfully disagrees, at least because the combination of Sosnowski and Eckhardt is improper, as discussed above.

Claims 9 and 34 and 25 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski in view of Eckhardt and further in view of Anderson. Applicant respectfully submits that this rejection is further addressed above with regard to claims 9, 34, and 25.

Claims 26 and 2, 7-9, 27-31, and 34 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski in view of Eckhardt and Anderson. Applicant respectfully submits, as discussed above, that the combination of Sosnowski and Eckhardt is improper. Further, Applicant has discussed the further combination of Anderson above. Accordingly, Applicant submits that claims 26, 2, 7-9, 27-31 and 34 are patentable over the cited art.

#### **New Claims**

**Serial No.:** 09/904,175

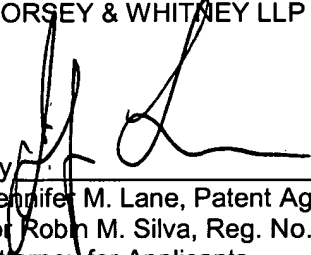
**Filing Date:** 11 JULY 2001

Applicant has added new claims 36-41 which further distinguish over the cited art. For example, claims 36 and 37 recite further limitations regarding a printed circuit board not disclosed by the cited art. Claim 38 recites an assay complex comprising an electron transfer moiety. Claims 39-41 recite a conductive oligomer, a gold electrode, and a thiol-containing monolayer forming species, respectively. The cited art fails to disclose these features, with Eckhardt specifically stating that "Metals such as gold having adsorbed thiols or disulfides cannot be used with this invention..." see col. 7, lines 7-9.

### **CONCLUSION**

Applicants submit the claims are in condition for allowance, and notification of such is respectfully requested. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,  
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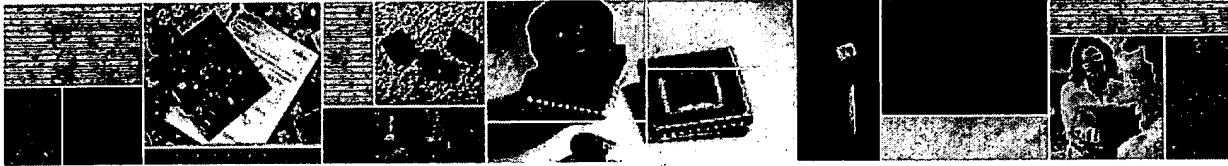
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## Dictionary

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Click on a letter then click on one of the acronyms displayed to see its definition. If the acronym you are looking for is not here, suggest a new entry by [e-mailing us](#).

[PABX](#) [PAM](#) [PCI](#) [PCM](#) [PCMCIA](#) [PC-NIC](#) [Pipeline processor](#)  
[PCN](#) [PDP](#) [PES](#) [PGA](#) [PHS](#) [PIC](#) [PICE](#) [PLA](#) [PLCC](#)  
[POTS](#) [PSK](#) [PSTN](#) [PWM](#)

**PABX - Private Automated Branch eXchange**

PABX - Private Automated Branch exchange

[Top of Page ▲](#)**PAM - Pulse Amplitude Modulation**

Pulse modulation in which the amplitude of the pulses is modulated by the corresponding samples of the modulating wave

[Top of Page ▲](#)**PCI - Peripheral Component Interconnect**

Industry standard bus interconnect specification - leading standard for PC add-ins

[Top of Page ▲](#)**PCM - Pulse Code Modulation**

Technique for digitising speech by sampling the sound waves and converting each sample into a binary number.

[Top of Page ▲](#)**PCMCIA - Personal Computer Memory Card International Association**

Standard for credit card-size adapter cards used in notebook computers. Applications include memory extensions, networking and modems.

[Top of Page ▲](#)**PCN - Personal Communications Network**

A European digital cellular type service.

[Top of Page ▲](#)**PDP - Plasma Display Panel**Colour display technology capable of creating large thin screens with wide viewing angle. [Click here](#) for more information[Top of Page ▲](#)**PES - Packetised Elementary Stream**

One of the input stream formats standardised by MPEG

[Top of Page ▲](#)**PGA - Pin-Grid Array (Programmable Gain Amplifier)**

Packaging technology for high-pin-count packages. Name derives from the array of pins at the bottom of the package. The pins go through holes on a



printed circuit board. I/O lead counts as high as 600 can be achieved with PGA packaging designs.

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### **PHS - Personal Handy phone System**

Versatile cordless/mobile system developed in Japan and increasingly popular elsewhere, e.g. Germany.

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### **PC-NIC - PC Network Interface Card**

Often abbreviated as NIC, an expansion board you insert into a computer so the computer can be connected to a network. Most NICs are designed for a particular type of network, protocol, and media, although some can serve multiple networks.

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### **Pipeline processor**

Faster way of processing data. Pipelining means inputting a second instruction before completion of processing the first

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### **PIC - Peripheral Interface Controller**

Low-end microcontrollers mainly used in domestic appliances and industrial systems. As with other micros, they make the product more intelligent and easier to use. PIC chips are programmed to perform only one very specific task, but altering the software program allows the same PIC chip to be used for different tasks. More information about Fujitsu MCUs is in the [Micros](#) section of this Web site.

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### **PICE - Personal In Circuit Emulator**

Microcontroller development tool. See also [ICE](#). More information about development tools is in the [Micros](#) section of this Web site.

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### **PLA - Programmable Logic Array**

Architecture using a programmable AND array in series with a programmable OR array.

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### **PLCC - Plastic Leaded Chip Carrier**

A leaded quad package - a replacement for the plastic DIP (dual in-line package) in surface-mount applications. External connections consist of leads around all four sides of the package.

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### **PSK - Phase Shift Keying**

Modulation technique used e.g. in satellite TV broadcasting. The quad PSK demodulator developed by Fujitsu is a successful implementation of [mixed signal technology](#). See our [multimedia devices](#) section

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### **PSTN - Public Switched Telephone Network**

PSTN - Public Switched Telephone Network.

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### **PWM - Pulse Width Modulation**

Form of analogue control in which the duration of digital pulses is varied analogously with the signal of interest. PWM is a popular feature of Fujitsu [microcontrollers](#)

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